Annals of Clinical and Analytical Medicine
Original Research

Association between gastric abnormalities and cholelithiasis: A cross-sectional study

Medeni Sermet
Department of General Surgery, Faculty of Medicine, Medeniyet University, Goztepe Prof. Dr. Suleyman Yalcin City Hospital, Istanbul, Turkey

Abstract

Aim: The study aims to reveal the relationship between the most common abnormalities of the upper digestive tract and cholelithiasis.

Materials and Methods: This cross-sectional study included 7651 patients, of whom 14318 tested positive for Helicobacter pylori (H. Pylori). Patients who underwent abdominal ultrasonography (USG) and esophagogastroduodenoscopy (between January 2014 and June 2022) were included. The following gastroesophageal conditions were examined to determine whether they affect the risk of cholelithiasis: atrophic gastritis (AG), gastric polyps, esophagitis, bile reflux, gastric ulcers, gastric mucosal erosion, superficial gastritis, and gastric H. Pylori infection. Logistic regression was used to calculate the unadjusted and adjusted odds ratios (OR) of H. Pylori infection for cholelithiasis occurrence. In addition, we examined whether AG influences the association between cholelithiasis and H. Pylori infection.

Results: A total of 8753 patients (61.1%) were diagnosed with cholelithiasis. Multivariate logistic regression analysis showed that H. Pylori infection (OR 1.28; 95% CI 1.10-1.42) and atrophic gastritis (OR 1.38; 95% CI 1.21-1.41) were significantly associated with cholelithiasis, as were age, female gender (OR 1.82; 95% CI 1.56-2.01), gastric polyps (OR 1.45; 95% CI 1.06-1.82). No additional interaction was observed between H. Pylori infection and AG; however, the overall effect on the risk of cholelithiasis was only slightly greater than the sum of the individual effects.

Discussion: Gastric disorders, such as gastric polyps, H. Pylori infection, and AG, increase the risk of cholelithiasis. However, there was no association between the development of cholelithiasis and esophagitis, bile reflux, erosive gastritis, gastric ulcers, or superficial gastritis.

Keywords

Cholelithiasis, Helicobacter Pylori, Gastritis, Atrophy, Gastric Polyp

DOI: 10.4328/ACAM.22017 Received: 2023-10-18 Accepted: 2023-11-20 Published Online: 2024-01-03 Printed: 2024-02-01 Ann Clin Anal Med 2024;15(2):117-121
Corresponding Author: Medeni Sermet, Department of General Surgery, Faculty of Medicine, Medeniyet University, Goztepe Prof. Dr. Suleyman Yalcin City Hospital, Istanbul, Turkey.
E-mail: sermetmedeni@gmail.com P: +90 507 236 70 20
Corresponding Author ORCID ID: https://orcid.org/0000-0001-6119-0037
This study was approved by the Ethics Committee of Istanbul Medeniyet Univesity (Date: 2022-07-22, No: 254)

Introduction

Cholelithiasis is a common digestive disease with a high incidence and relatively low mortality [1]. Cholelithiasis is one of the most common diseases and its prevalence is increasing worldwide [2].

Although cholelithiasis is the result of a complex interaction of genetic, environmental, metabolic, and related conditions, factors such as advanced age and sex cannot be modified. Diet and physical activity may be modifiable risk factors [3].

Although there are numerous studies on the risk factors of cholelithiasis, there is a lack of data on its association with benign diseases of the stomach.

One-third of detected cholelithiasis cases are symptomatic. Similar symptoms were observed in gastric pathologies. Although several studies have examined the relationship between H. Pylori infection and the risk of cholelithiasis, the results are still controversial [4, 5]. On the other hand, the relationship between gastric pathologies such as AG, superficial gastritis, gastric polyps, bile reflux, esophagitis with gallstone formation is unknown.

Today, the easy accessibility of esophagogastroduodenoscopy (EGD) and ultrasonography (USG) procedures facilitates the diagnosis and treatment of gastric and gallbladder diseases.

Large population-based cohort studies are rare in the research literature on factors associated with gallstones [5, 6]. Therefore, we performed a retrospective analysis of a database of 65451 patients who underwent EGD to identify possible associations between cholelithiasis and various upper gastrointestinal diseases. We also examined the effect of the association between AG and H. Pylori infection in cholelithiasis.

Material and Methods

Study Participants

We conducted a cross-sectional study of patients who underwent EGD and USG at our facility between January 2014 and June 2022. During this period, 65451 patients underwent gastroscopy and 107218 patients underwent USG. We included 15840 patients with a maximum interval of six months between EGD and USG. For repeated endoscopies, only the initial data were considered.

We excluded 1522 patients for the following reasons.

1) If the time between EGD and USG was more than 6 months
2) Technically inadequate or incomplete endoscopy
3) Gastrointestinal surgery.
4) Diagnosis revealed gastrointestinal tumors.
5) Continuous PPI and anti-ulcer drug use
6) Diagnosis of acute cholecystitis, choledocholithiasis, and cholangitis.

Finally, 14318 participants were included in the analysis. (Figure 1).

A patient flowchart is shown in Figure 1.

Gastrointestinal (GI) tract endoscopic examinations were performed by specialized gastroscopists. The endoscopy center database contains descriptive endoscopic findings. The presence or absence of gastric mucosal atrophy, gastric polyps, esophagitis, bile reflux, gastric ulcers, gastric mucosal erosion, and superficial gastritis were considered significant gastric disorders. The diagnostic criteria for the listed disorders were based on endoscopic and pathological findings.

Analytical Statistics

Categorical data are summarized as frequency (%) and continuous variables as mean standard deviation (SD). The chi-square test and Mann-Whitney U-test were used for group comparisons. Collinearity between the gastric variables was examined using variance inflation factors, and no correlation was found.

Univariate logistic regression analysis was used to determine the association between gastric outcomes and cholelithiasis. Variables with $P < 0.1$ were then added to a multivariate analysis. OR and 95% CI were used to determine results. Statistical significance was set at $P < 0.05$. Data analysis was performed using R 4.1.2 and SPSS statistics version 23.

The effects we also examined whether the combined effect of H. Pylori infection or AG on cholelithiasis were greater than the sum of the individual effects of each factor. Individuals were divided into four groups according to their H. Pylori and AG status: H. Pylori (-) and AG (-), H. Pylori (−), AG (+), H. Pylori (+), AG (−), H. Pylori (+) and AG (+). Using the H. Pylori (-) and AG (-) groups as the reference analysis, we calculated the ORs of the other three categories. We assessed the occurrence of additional interactions by calculating the synergy index (SI), attributable rate (AP) due to interaction, and relative excess risk (RR) due to interaction. The 95% CI of RR and AP were > 0 and the 95% CI of SI was > 1, indicating a positive interaction; the 95% CI of RR and AP included 0 [7].

Ethical Approval

This study was approved by the Ethics Commitee of Istanbul Medeniyet Univesity (Date: 2022-07-22, No: 254).

Results

Common features of the topics

Of the 14318 registered cases, 8753 (61,1%) had cholelithiasis. Of the study population, 60.5% were female, and the mean age was 52,3 years.

Table 1 lists the clinical characteristics of the participants with cholelithiasis and the controls without cholelithiasis. Age is expressed as mean (SD), and all other data are expressed as number (proportion).

Compared with the group without cholelithiasis, patients with cholelithiasis were older and had a female-to-male sex ratio of 1.52. They also had higher rates of atrophic gastritis,

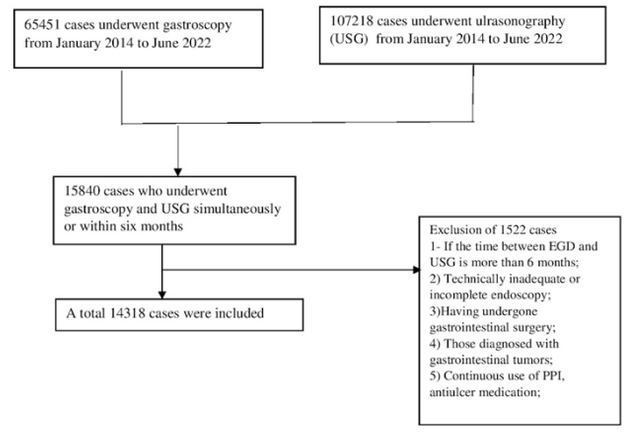

Figure 1. Study design

esophagitis, alkaline bile reflux, gastric polyps, gastric ulcers, erosive gastritis, superficial gastritis, and Helicobacter pylori infection.

The findings of logistic regressions of the two study populations are shown in Table 2.

One included all 14318 study participants, while the other included 7651 cases with H. Pylori (+) data. Univariate analyses of the two populations were performed. All studies showed that the risk of cholelithiasis was significantly influenced by age, sex, gastric polyps, esophagitis, gastric ulcer, erosive gastritis, superficial gastritis, AG, and H. Pylori.

Multivariate analysis included all indicators of the univariate analysis (Table 2) (P <0.1). The findings showed that age, sex, gastric polyps, H. Pylori infection, and AG were independent risk

Table 1. General characteristics of patients with and without cholelithiasis

Parameters	(n=14318)	Cholelithiasis (+) (n=8753)	Cholelithiasis (-) (n=5565)	P Value
Gender (Female/Male)	8753(%60.5)/ 5565 (%39.5)	5351 (%61.1)/ 3402 (%38.9)	3306 (%59.4)/ 2259 (%40.6)	<0,001
Age (years)	52.3 (18-87)	54.9 (19-87)	47.7 (18-85)	<0,001
Athrofic gastritis	3579 (24.9%)	1912 (21.8%)	1657 (29.8%)	<0,001
Esophagitis	1108 (7.7%)	712 (8.1%)	396 (7.2%)	<0,001
Gastric ulcus	2254 (15.7%)	1520 (17.4%)	734 (13.2%)	<0,001
Bile reflux	715 (4.9%)	534 (6.1%)	181 (3.2%)	<0,001
Erozive gastritis	7849 (54.8%)	4042 (46.2%)	3807 (68.4%)	<0,001
Superficial gastritis	4772 (33.3%)	3521 (24.6%)	1251 (22.4%)	<0,001
Helicobacter pylori (+)	7651 (53.4%)	4599 (52.5%)	3052 (54.8%)	<0,001
Gastric polyp	312 (2.2%)	183 (2.1%)	129 (2.3%)	<0,001

Table 2. Univariate analysis for risk of cholelithiasis

Parameters	Univariate analysis (N=14318) OR (95% Confidence Interval)	P Value	Univariate analysis (N=7651) OR (95% Confidence Interval)	P Value
Age (years)	1.06 (1.06-1.06)	<0.001	1.06 (1.06-1.07)	<0.001
Gender (Female/Male)	1.64 (1.56-1.73)	<0.001	1.57 (1.41-1.69)	<0.001
Atrophic gastritis	1.72 (1.63-1.81)	<0.001	1.83 (1.64-2.05)	<0.001
Esophagitis	1.38 (1.30-1.47)	<0.001	1.29 (1.11-1.52)	<0.001
Gastric ulcer	1.24 (1.16-1.32)	<0.001	1.19 (1.04-1.34)	0.018
Bile reflux	0.82 (0.76-0.85)	<0.001	0.77 (0.62-0.98)	0.061
Erozive gastritis	1.41 (1.36-1.47)	<0.001	1.38 (1.22-1.51)	<0.001
Superficial gastritis	0.62 (0.60-0.66)	<0.001	0.63 (0.57-0.70)	<0.001
Helicobacter pylori pozitive	1.25 (1.16-1.42)	<0.001	1.24 (1.13-1.41)	<0.001
Gastric polyp	1.81 (1.76-1.96)	<0.001	1.83 (1.71-2.09)	<0.001

P < 0.01
Use a dicimal point (.) instead of comma to represent a percentage and dicimal figures.
Include a row for p value.

Table 3. Multivariate analysis for the risk of cholelithiasis

Parameters	Cholelithiasis (+) (N=8753)	Cholelitiasis(-) (N=5565)	OR (95%)	P value
Age (years)				
Q1 (<40)	1418 (16.2)	1864 (33.5)	1	
Q2 (40-50)	2205 (25.2)	1631 (29.3)	1.84 (1.67-2.15)	<0.001
Q3 (50-60)	2415 (27.6)	1341 (24.1)	2.64 (2.32-2.99)	<0.001
Q4 (>60)	2721 (31.2)	729 (13.1)	3.27 (2.82-3.96)	<0.001
Gender (Female/Male)	5357 (61.2)	3250 (58.4)	1.82 (1.56-2.01)	<0.001
	3396 (38.8)	2315 (41.6)	1.67 (1.44- 1.96)	<0.001
Atrophic gastritis	1912 (21.8%)	1657 (29.8%)	1.36 (1.21-1.41)	<0.001
Esophagitis	712 (8.1%)	396 (7.2%)	1.14 (0.85-1.44)	0.124
H.Pylori	4599 (52.5%)	3052 (54.8%)	1.28 (1.10-1.42)	<0.001
Gastric ulcer	2254 (25.7%)	1520 (17.4%)	1.06 (0.96-1.22)	0.631
Bile reflux	715 (8.2%)	534 (9.6%)	0.91 (0.76-1.16)	0.787
Erozive gastritis	4042 (46.2%)	3807 (68.4%)	1.11 (0.96-1.27)	0.328
Superficial gastritis	3521 (40.2%)	1251 (22.4%)	0.98 (0.81-1.10)	0.255
Gastric polyp	183 (2.1%)	129 (2.3%)	1.45 (1.06-1.82)	0.012

P < 0,01
Effects of H.pylori infection and AG on cholelithiasis, separately and in combination

factors for cholelithiasis. We also performed a trend test and stratified age into four quartiles with 10-year intervals. An OR of 3.27 (95% CI, 2.82-3.96) (P for trend 0.001) was observed in those in the highest age quartile (> 60) (Table3).

The incidence of cholelithiasis was 27.5% in AG (-) and H. Pylori (-) patients, 34,9% in H. Pylori (+) and AG (-) patients, 44,9% in AG (+) and H. Pylori (-) patients, and 55.6% in AG (+) and H. Pylori (+) patients. People with AG (OR: 1.78, 95% CI: 1.56-2.05) had a higher incidence of cholelithiasis than people without atrophy and without H. Pylori infection, while people with H. Pylori infection (OR: 1.13, 95% CI: 0.99-1.30) had a lower incidence of cholelithiasis.

However, the relative excess risk attributed to the interaction was not statistically significant (RR: 0.14 (-0.31-0.55), AP: 0.07 (-0.14-0.26), SI: 1.14 (0.72-1.71). In addition, H. Pylori infection and AG were associated with a high risk of developing cholelithiasis.

Discussion

In this study, the USG and typical EGD findings of 14318 individuals were compared. These findings suggest that individuals with sex, age, gastric polyps, AG, and H. Pylori infection have an increased risk of developing cholelithiasis. In addition, individuals with concurrent AG and H. Pylori infections may have an even higher chance of developing cholelithiasis.

Recently, the link between H. Pylori infection and cholelithiasis has attracted the attention of several researchers [8, 9, 10]. However, these results have not yet been conclusive. Although a number of studies have found a link between H. Pylori and cholelithiasis, other studies have found no link between the two [11, 12]. We hypothesized that these inconsistent findings may be partly related to the various H. Pylori detection techniques, geographic regions, racial groups, and small sample sizes. Based on 477293 individuals in a nationwide database, a very large prospective analysis was performed to evaluate the association between cholelithiasis and the effect of gastric acid-suppressive drugs on gallbladder histology. The results showed an association with increased gallstone formation [13], whereas a retrospective cohort of 27881 individuals preliminarily evaluated the presence of H. Pylori and concluded that it may not be associated with the development of gallstones [14].

According to a previous study, the risk of developing cholelithiasis was higher in people with intestinal metaplasia, gastric polyps, and H. Pylori infection, and findings showed that AG is an important parameter for cholelithiasis [15].

Recently, it has been hypothesized that H. Pylori infection is associated with a higher risk of developing cholelithiasis when coexisting with chronic AG [16]. In our study, we found that the combined effects of H. Pylori infection and AG on cholelithiasis were only slightly greater than those of each factor individually. Therefore, we hypothesized that H. Pylori and AG may interact together and conducted additional research to support this hypothesis. Therefore, we performed additional tests for erosive and superficial gastritis. Although our data showed a positive additive interaction between these two factors and the likelihood of cholelithiasis, this was not statistically significant. However, we still recommend, especially in patients with AG, that H. Pylori eradication may reduce the prevalence of cholelithiasis; however, this needs to be confirmed in the future [17]. In addition, cholelithiasis was independently linked to AG without H. Pylori infection but not solely to H. Pylori infection alone.

As most AGs are typically caused by H. Pylori infection, prolonged H. Pylori infection may be more important for the development of cholelithiasis.

Other theories have been proposed to explain the mechanisms underlying the association between H. Pylori infection and cholelithiasis. First, H. Pylori infection and AG cause hypergastrinemia, which may help in the development of cholelithiasis by promoting gallbladder mucosal damage [18]. Some studies have found a link between gastrin and cholelithiasis, while others have found the opposite [19, 20]. Second, persistent H. Pylori infection causes chronic AG by reducing acid secretions. Low gastric acid levels can alter the gastrointestinal microbiota and cause bacterial overgrowth, which may contribute to the development of cholelithiasis [20, 21].

Several studies have revealed that the detection rate of H. Pylori in cholecystectomy is higher than in normal mucosa [21, 22]. Consequently, H. Pylori may locally trigger cholelithiasis by contacting the mucosa.

In a cohort study, the prevalence of cholelithiasis was higher in individuals with gastric polyps [22]. However, the mechanisms involved remain unclear. The majority of gastric fundic gland polyps, which constitute the majority of gastric polyps, are symptoms associated with long-term proton pump inhibitor therapy [23]. Polyps may develop as a result of a decrease in the gastric acid barrier. Gastric polyps are closely associated with H. Pylori infection and atrophic gastritis; however, the physiopathologic explanation for this association is still unclear [24]. Another hypothesis is that lifestyle, environmental and hereditary factors may significantly influence the mechanism underlying this association [24]. In our study, the presence of gastric polyps was more common in patients with H. Pylori, and a significant association with cholelithiasis was found in parallel.

We understand that the risk of cholelithiasis is higher in females and older participants. Similarly, our study found that women were more likely to develop cholelithiasis than men were. In addition, the prevalence of cholelithiasis increases over time with age, with the highest OR 3.27; 95% CI: 2.82-3.96) seen in the older age group.

Therefore, it is necessary to discuss possible flaws in this study. First, because the present analysis is based on histological diagnoses and endoscopic findings, there may be subjectivity and diagnostic variability among observers. Although the lesions were described on endoscopy, the endoscopists did not biopsy every lesion. However, our endoscopists applied a standardized algorithm that enabled them to report similar interpretations on similar images.

Second, because the study was retrospective, we were unable to collect data on dietary patterns, lifestyle choices, medical history, substance use, and other confounding variables, but in other studies these confounding variables have had little or no effect on these associations [25]. Third, we used data from only

one data center; therefore, different groups should establish the generalizability of our findings. Despite these drawbacks, our study is the first to examine the link between cholelithiasis and endoscopically detected gastric abnormalities using a large sample size.

Independent risk factors for cholelithiasis include gastrointestinal diseases such as gastric polyps, H. Pylori infection, and AG. In addition, the combination of AG and H. Pylori infections may cause a marginal increase in the risk of developing cholelithiasis. However, it is likely that the presence of cholelithiasis is not associated with conditions such as esophagitis, bile reflux, gastric mucosal erosion, gastric ulcers, and superficial gastritis. Therefore, screening ultrasonography should be considered when individuals are found to have gastric polyps, AG, or H. Pylori infection after EGD.

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

Funding: *None*

Conflict of Interest

The authors declare that there is no conflict of interest.

References

1. Dan WY, Yang YS, Peng LH, Sun G, Wang ZK. Gastrointestinal microbiome and cholelithiasis: Current status and perspectives. World J Gastroenterol. 2023;29(10):1589-601.

2. Pak M, Lindseth G. Risk factors for cholelithiasis. Gastroenterol Nurs. 2016;39(4):297-309.

3. Fatemi S. M, Doosti A, Shokri D, Ghorbani-Dalini S, Molazadeh M, Tavakoli et al. Is There a correlation between helicobacter pylori and enterohepatic helicobacter species and gallstone cholecystitis?. Middle East J Dig Dis. 2018;10(1):24-30.

4. Hjaltadottir K, Haraldsdottir KH, Moller PH. Gallstones-review. Laeknabladid. 2020;106(10):464-72.

5. Di Ciaula A, Garruti G, Frühbeck G. The role of diet in the pathogenesis of cholesterol gallstones. Curr Med Chem. 2019;26(19):3620-38.

6. Patel A. M, Yeola M, Mahakalkar C. Demographic and risk factor profile in patients of gallstone disease in central India. Cureus, (2022);14(5),e24993.

7. Toneyan S, Tang Z, Koo PK. Evaluating deep learning for predicting epigenomic profiles. Nat Mach Intell. 2022;4(12):1088-100.

8. Kunnuru SKR, Kanmaniyan B, Thiyagarajan M, Singh BK, Navrathan N. A Study on efficacy of UGI scopy in cholelithiasis patients before laparoscopic cholecystectomy. Minim Invasive Surg. 2021;2021:8849032.

9. Zhang, F. M, Yu C. H, Chen H. T, Shen Z, Hu F. L, et al. Helicobacter pylori infection is associated with gallstones: Epidemiological survey in China. World journal of gastroenterology, 2015;21(29), 8912–9.

10. Ari A, Tatar C, Yarikkaya E. Relationship between Helicobacter pylori-positivity in the gallbladder and stomach and effect on gallbladder pathologies. J Int Med Res. 2019;47(10):4904-10.

11. Wang L, Chen J, Jiang W, et al. The relationship between helicobacter pylori Infection of the gallbladder and chronic cholecystitis and cholelithiasis: A systematic review and meta-analysis. Can J Gastroenterol Hepatol. 2021;2021:8886085.

12. Dellon ES, Hirano I. Epidemiology and natural history of eosinophilic esophagitis. Gastroenterology. 2018;154(2):319-32.

13. Yang M, Xia B, Lu Y, et al. Association between regular use of gastric acid suppressants and subsequent risk of cholelithiasis: A prospective cohort study of 0.47 million participants. Front Pharmacol. 2022;12:813587.

14. Zhang J, Zhang Y, Chen Y, Chen W, Xu H, Sun, W. et al. Helicobacter pylori is not a contributing factor in gallbladder polyps or gallstones: a case-control matching study of Chinese individuals. The Journal of international medical research. 2020;48(10), 300060520959220.

15. Santos M. L. C, de Brito B. B, da Silva F. A. F, Sampaio M. M, Marques, et al. (2020). Helicobacter pylori infection: Beyond gastric manifestations. World journal of gastroenterology, 26(28), 4076–93.

16. Grigor'eva IN, Romanova TI. Gallstone disease and microbiome. Microorganisms. 2020;8(6):835.

17. Lee S. H. Jang,D. K. Yoo,M. W, Hwang S. H, Ryu S. Y, Kwon O. K, et al. Efficacy and safety of ursodeoxycholic acid for the prevention of gallstone formation after gastrectomy in patients with gastric cancer: The PEGASUS-D randomized clinical trial. JAMA Surg. 2020;155(8):703-11.

18. Sharndama HC, Mba IE. Helicobacter pylori: an up-to-date overview on the virulence and pathogenesis mechanisms. Braz J Microbiol. 2022;53(1):33-50.

19. Faridi MS, Jaiswal MS, Goel SK. Expression of CCK receptors in carcinoma gallbladder and cholelithiasis: A pilot study. J Clin Diagn Res. 2015;9(7):PC04-PC7.

20. Guraya SY, Ahmad AA, El-Ageery SM. The correlation of helicobacter pylori with the development of cholelithiasis and cholecystitis: the results of a prospective clinical study in Saudi Arabia. Eur Rev Med Pharmacol Sci. 2015;19(20):3873-80.

21. Carmack SW, Genta RM, Schuler CM, Saboorian MH. The current spectrum of gastric polyps: a 1-year national study of over 120,000 patients. Am J Gastroenterol. 2009;104(6):1524-32.

22. Cen L, Wu J, Zhu S, Pan J, Zhou T, Yan T, et al. The potential bidirectional association between Helicobacter pylori infection and gallstone disease in adults: A two-cohort study. Eur J Clin Invest. 2023;53(2):e13879.

23. Svistunov AA, Osadchuk MA, Mironova ED, Guliaev PV, Vasileva IN. Ter Arkh. 2022;94(2):194-9.

24. Abraham SC, Singh VK, Yardley JH, Wu TT. Hyperplastic polyps of the stomach: associations with histologic patterns of gastritis and gastric atrophy. Am J Surg Pathol. 2001;25(4):500-7.

25. Li L, Tan J, Liu L, Li J, Chen G, et al. Association between H. pylori infection and health Outcomes: an umbrella review of systematic reviews and meta-analyses. BMJ Open. 2020;10(1):e031951.

How to cite this article:

Medeni Sermet. *Association between gastric abnormalities and cholelithiasis: A cross-sectional study. Ann Clin Anal Med 2024;15(2):117-121*

This study was approved by the Ethics Committee of Istanbul Medeniyet Univesity (Date: 2022-07-22, No: 254)